



Practical Management Guide for Clinicians Who Treat Patients with Amiodarone

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ABSTRACT

Amiodarone, an iodinated benzofuran derivative with Class I, II, III, and IV antiarrhythmic properties, is the most commonly used antiarrhythmic drug used to treat supraventricular and ventricular arrhythmias. Appropriate use of this drug, with its severe and potentially life-threatening adverse effects, requires an essential understanding of its risk-benefit properties in order to ensure safety. The objective of this review is to afford clinicians who treat patients receiving amiodarone an appropriate management strategy for its safe use. The authors of this consensus management guide have thoroughly reviewed and evaluated the existing literature on amiodarone and apply this information, along with the collective experience of the authors, in its development. Provided are management guides on the intravenous and oral dosing of amiodarone, appropriate outpatient follow-up of patients taking the drug, its recognized adverse effects, and recommendations on when to consult specialists to help in patient management. All clinicians must be cognizant of the appropriate use, follow-up, and adverse reactions of amiodarone. The responsibility incurred by those treating such patients cannot be overemphasized.

Published by Elsevier Inc. • *The American Journal of Medicine* (2016) 129, 468-475

KEYWORDS: Adverse drug reactions; Amiodarone; Atrial fibrillation; Ventricular fibrillation; Ventricular tachycardia

Amiodarone is the most commonly used antiarrhythmic drug to treat supraventricular and ventricular arrhythmias.¹⁻³

Because of severe and potentially life-threatening adverse drug reactions, careful use is essential to derive optimal benefits from the drug with the least risk. This guide updates a version published in 2007,⁴ reviews indications for use, and recommends strategies to ensure safe drug use. Recommendations are based on a thorough and careful evaluation of the literature and the collective experience of the writing committee.

Funding: None.

Conflict of Interest: No author has any conflict of interest related to this work.

Authorship: All authors had access to the data and actively participated in writing this manuscript.

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INDICATIONS FOR USE

Oral Amiodarone

Ventricular Arrhythmias. Oral amiodarone was approved by the Food and Drug Administration (FDA) for the treatment of life-threatening, recurrent ventricular arrhythmias, such as ventricular fibrillation or ventricular tachycardia associated with hemodynamic instability. Oral dosing may require a high-dose load to achieve efficacy.

Prospective trials have shown long-term neutral, if not encouraging, impact of amiodarone on survival in patients after myocardial infarction with left ventricular systolic dysfunction and with dilated cardiomyopathy.⁵⁻⁹ A meta-analysis showed a 10%-19% reduction in mortality in high-risk patients given amiodarone.¹⁰ A subsequent meta-analysis reported amiodarone to have neutral effect on survival but was associated with a two- to fivefold increased risk of pulmonary and thyroid toxicity.¹¹ One prospective analysis indicated that amiodarone may adversely affect

survival in patients with New York Heart Association functional class III heart failure.¹²

Implantable cardioverter-defibrillators are superior to amiodarone to improve survival in patients with sustained ventricular tachycardia or ventricular fibrillation due to a nonreversible cause and in patients at high risk for sudden cardiac death (selected postmyocardial infarction and cardiomyopathy patients).^{12,13} Amiodarone is the antiarrhythmic drug of choice for patients with ventricular tachycardia or ventricular fibrillation who are not otherwise candidates for an implantable cardioverter-defibrillator. This is based on the drug's efficacy,^{10,14,15} its minimal negative inotropic effects,¹⁶ and its low proarrhythmic potential.¹⁷ Concomitant antiarrhythmic therapy, most commonly amiodarone, is used to treat atrial and ventricular arrhythmias in 30%-70% of patients with an implantable cardioverter-defibrillator. It has been shown that amiodarone, combined with a beta-blocker, reduced frequent implantable cardioverter-defibrillator shocks.¹⁸ Amiodarone can also suppress symptomatic, nonsustained ventricular tachycardia.

Atrial Fibrillation. Although amiodarone is not FDA-approved to treat atrial fibrillation, it is commonly used for this purpose. Due to the drug's long half-life and large volume of distribution, oral dosing to achieve efficacy may take days to weeks. The 1-year efficacy to maintain sinus rhythm exceeds other antiarrhythmic drugs. In one prospective trial, 65% of patients taking amiodarone vs 37% taking sotalol or propafenone remained in sinus rhythm.¹⁹ Amiodarone should be considered only after failure of, or contraindications to, other drugs due to its potential for end-organ toxicity. Per American College of Cardiology/American Heart Association/Heart Rhythm Society guidelines,²⁰ amiodarone can be used to help maintain sinus rhythm for patients after myocardial infarction, with heart failure, left ventricular systolic dysfunction, left ventricular hypertrophy, or with drug-refractory symptomatic atrial fibrillation. Amiodarone may prevent atrial fibrillation following cardiac surgery,^{21,22} but preoperative prophylactic amiodarone has not been universally accepted due to logistical problems of preoperative loading, minimal effect on length of stay, concerns for potential toxicity, and cost. Although amiodarone can slow the ventricular response in atrial fibrillation, it should be used only after digoxin, beta-blockers, and calcium channel antagonists are ineffective, contraindicated, or not tolerated.

Intravenous Amiodarone

Intravenous amiodarone can treat atrial and ventricular arrhythmias. Even though tissue levels increase rapidly, effective arrhythmia suppression and prevention can take days or longer. Sinus bradycardia, atrioventricular block, and rarely, torsades de pointes ventricular tachycardia occur following intravenous loading.

CLINICAL SIGNIFICANCE

- Amiodarone is the most commonly used antiarrhythmic drug to treat supraventricular and ventricular arrhythmias.
- Because of severe and potentially life-threatening adverse drug reactions, careful use is essential to derive optimal benefits from the drug with the least risk.
- This guide updates a version published in 2007, reviews indications for use, and recommends strategies to ensure safe drug use.
- Recommendations are based on a thorough and careful evaluation of the literature and the collective experience of the writing committee.

Ventricular Arrhythmias. Intravenous amiodarone is FDA-approved for treatment and prophylaxis of recurrent ventricular fibrillation and hemodynamically unstable ventricular tachycardia, and to suppress and prevent ventricular fibrillation or ventricular tachycardia in patients who are candidates for oral amiodarone but unable to take the oral preparation. Based on the 2010 Advanced Cardiac Life Support guidelines, intravenous amiodarone is indicated as the antiarrhythmic drug of first choice for persistent ventricular fibrillation or pulseless ventricular tachycardia resistant to other resuscitative measures including epinephrine.²³ However, in 2

prospective double-blind studies that evaluated intravenous amiodarone for shock-resistant out-of-hospital cardiac arrest,^{24,25} amiodarone was associated with a greater chance of survival to hospital admission but there was no survival benefit to hospital discharge.

Amiodarone can treat lidocaine-refractory ventricular tachycardia or ventricular fibrillation after acute myocardial infarction, "electrical storm" (ie, multiple episodes of recurrent rapid ventricular tachycardia or ventricular fibrillation requiring multiple defibrillations over a short time period), and nonsustained and recurrent ventricular tachycardia in patients with implantable cardioverter-defibrillators who experience frequent device shocks.²⁶

Atrial Fibrillation and Other Supraventricular Arrhythmias. Intravenous amiodarone can treat supraventricular tachyarrhythmias, most commonly atrial fibrillation, in acute settings, including perioperative cardiovascular surgery, in intensive care units, and in emergency departments.²⁷⁻²⁹ While it can slow the ventricular response during acute-onset atrial fibrillation,²⁸ it is not FDA-approved for this use. In placebo-controlled trials, intravenous amiodarone has not been shown to convert atrial fibrillation acutely.^{29,30} In a prospective active-control trial against vernakalant, intravenous amiodarone converted only 5.2% of patients with persistent atrial fibrillation to sinus rhythm within 90 minutes.³¹ Although it can reduce atrial fibrillation occurrence after cardiac surgery,^{32,33} a beneficial

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